

July 1st 2022

Position statement from the ENTIS Scientific Committee & Board

Summary: In March 2022 the European Medicines Agency's (EMA) published a direct healthcare professional communication (DHPC) regarding the use of live vaccines in infants exposed to infliximab *in utero* or during breastfeeding.

The marketing authorization holders of infliximab, in agreement with the EMA and the National Competent Authority state that:

- live vaccines (e.g. BCG vaccine) should not be given to infants after *in utero* exposure to infliximab for 12 months after birth. If there is a clear clinical benefit for the individual infant, administration of a live vaccine might be considered at an earlier timepoint if infant infliximab serum levels are undetectable or if infliximab administration was limited to the first trimester of pregnancy
- administration of a live vaccine to a breastfed infant while the mother is receiving infliximab is not recommended unless infant infliximab serum levels are undetectable

ENTIS response:

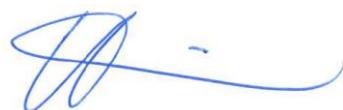
- One-year avoidance of live vaccines (instead of 6 months) in infants following late pregnancy exposure to infliximab is not sufficiently substantiated. This is a real concern in a time when the vaccines in question are becoming more relevant. Evidence for harm in humans is described in a small number of infants after BCG administration, whose mothers had been treated with infliximab late in pregnancy.^{1,2}
- Detection of minute concentrations of infliximab in breastmilk³ of some women and in infant serum after exposure via breastmilk, does not necessarily represent significant clinical risk after live vaccine administration to the infant. These levels were not high enough to anticipate systemic immunosuppression. Furthermore, we know that absorption from the GI tract of the infant is minimal. It is important to encourage breastfeeding, it has proven health and wellbeing benefits for both the infant and mother.
- The recommendation to measure serum infliximab levels among infants, whose mothers are treated with infliximab, is neither practical nor ethical.
- These recommendations do not serve to enhance women's or infant's health. We therefore strongly encourage the Pharmacovigilance Risk Assessment Committee - PRAC & EMA to reconsider these updated recommendations.

1. Cheent K, Nolan J, Shariq S, Kiho L, Pal A, Arnold J. Case Report: Fatal case of disseminated BCG infection in an infant born to a mother taking infliximab for Crohn's disease. *J Crohns Colitis* 2010; **4**(5): 603-5.
2. Chua N, Parker E, Giles I, Goulden B. A systematic review of live vaccine outcomes in infants exposed to biologic disease modifying anti-rheumatic medications (DMARDs) in-utero. *Rheumatology (Oxford)* 2022.
3. Fritzsche J, Pilch A, Mury D, Schaefer C, Weber-Schoendorfer C. Infliximab and adalimumab use during breastfeeding. *J Clin Gastroenterol* 2012; **46**(8): 718-9.

Signed by,

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